International Surgery Journal
Orozco CAO et al. Int Surg J. 2022 Jul;9(7):1377-1382
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: https://dx.doi.org/10.18203/2349-2902.isj20221732

Review Article

The role of the pseudoexfoliative syndrome as a transitional entity to glaucoma

Cesar Alberto Ortiz Orozco[1]*, Felix Osuna Gutiérrez[2], José María Zepeda Torres[2], Carlos Navarro Fernandez[1], Adriana Baltazar Gomez[1], Sofia Vibiana Garcia Aguilar[1], Victor Manuel Elizarras Garcia[3]

[1]Hospital Civil de Guadalajara Dr Juan I Menchaca, Departamento de cirugía, Guadalajara, Jalisco, Mexico
[2]School of Medicine, Autonomous University of Guadalajara, Guadalajara, Jalisco, Mexico
[3]Departamento de Urgencias, Hospital General de Zona 14, Instituto Mexicano del Seguro Social, Guadalajara, Jalisco, Mexico

Received: 05 June 2022
Revised: 18 June 2022
Accepted: 20 June 2022

***Correspondence:**
Dr. Cesar Alberto Ortiz Orozco,
E-mail: cesar.ortiz08@gmail.com

ABSTRACT

The balance between the secretion of aqueous humor by the ciliary body and its drainage through 2 independent pathways, the trabecular meshwork and the uveoscleral outflow pathway; and this will determine the intraocular pressure, which is considered the determining factor for glaucoma. Glaucoma is an entity of great clinical importance, being the second cause of blindness worldwide. There are different explanations for the pathophysiology of the disease, as well as immunological and vascular factors that lead to an increase in intraocular pressure, causing all these factors to trigger the development of glaucoma. Pseudoexfoliation syndrome can be defined as a systemic pathology that is generated by the deposition of extracellular fibrillar material in different tissues, and which, depending on the affected person, can cause different subsequent entities. Glaucoma progression and its sequelae may be more related to higher intraocular pressures than to other mechanisms. Various studies relate oxidative stress to glaucomatous progression. As the composition of the material causing pseudoexfoliation is further studied, its influence on the eye can be better understood.

Keywords: Glaucoma, Pathophysiology, Pseudoexfoliative

INTRODUCTION

Under physiological conditions, the aqueous humor is generated at the level of the choroid plexuses of the ciliary body- these are prolongations of the ciliary bodies that synthesize and secrete aqueous humor-, by the irrigation of the choroid vessels. From here the water wave slides through the posterior chamber between the anterior face of the lens and the posterior face of the iris, and passing through the pupil, fills the anterior chamber. To go to the chamber angle and be eliminated through it, through 3 structures the trabecular tissue, which is a mesh through which the aqueous humor accesses Schlemm's canal, which is the second, and finally reaches the aqueous veins, the third, to finally be eliminated by the general circulation. As can be seen, this mechanism develops at the level of the anterior segment of the eye, precisely in the chamber angle or sinus.[1-8]

The balance between the secretion of aqueous humor by the ciliary body and its drainage through 2 independent pathways, the trabecular meshwork and the uveoscleral

outflow pathway; and this will determine the intraocular pressure, which is considered the determining factor for glaucoma.[1,2]

Glaucoma represents an irreversible degenerative optic neuropathy characterized by progressive degeneration of retinal ganglion cells and the retinal nerve fiber layer, leading to corresponding visual field defects. Although the major risk factor, and the only modifiable risk factor, for disease onset and progression is elevated intraocular pressure, the pathogenesis of the disease is multifactorial and not well understood.[9-13]

Glaucoma is the second common cause of blindness and 4.5 million people currently suffer from it with projections of 11 million affected by 2020, the World Health Organization (WHO) said today.[14]

It is estimated that 66.8 million people worldwide have glaucoma, and 6.7 million have bilateral blindness (207). In countries where there is an official registry of blindness, glaucoma represents from 6.7% to 21% of blindness. Without treatment, it can cause blindness in 5% of those affected.[15]

It was calculated in 2017 that by the year 2020 there could be 79.6 million people affected by glaucoma (74% with open-angle glaucoma), with bilateral blindness in 5.9 million people with open-angle glaucoma and 5.3 million people with glaucoma of closed angle. A figure that will increase to 111.8 million in 2040 approximately.[15]

There are different types of glaucoma, but the two main ones are “open angle” and “closed angle”. The pathophysiology of glaucomatous damage continues to be the subject of research, although some theories have been described that could explain these entities.[10,16]

In this text, glaucomas will be classified according to their etiology:

Depending on the cause, glaucomas can be classified as primary, secondary and congenital. The primary ones are not associated with ocular or systemic diseases that cause resistance of the aqueous humor drainage system or angle closure; On the other hand, secondary glaucomas are associated with eye and genetic diseases that prevent adequate drainage of aqueous humor. Primary glaucomas usually affect both eyes, while secondary ones usually affect only one. In congenital glaucomas, the drainage pathways of the aqueous humor suffered a defective development during pregnancy.[17,18]

In 1996, the American Academy of Ophthalmology first discussed the definition of open-angle glaucoma excluding both visual field defects and intraocular pressure; and instead considered the characteristic glaucomatous change in optic nerve or nerve fiber defects to be sufficient for its definition. Primary open angle glaucoma is the most common cause of glaucoma.[12,19]

Angle-closure glaucoma is caused by blockage of the ocular drainage, that is, the trabecular meshwork is unable to flow towards Schlemm's canal; occurs when the angle of the anterior chamber is occluded by the iris, which consequently increases intraocular pressure. It may be the result of several factors, including a relatively thicker and more anteriorly positioned lens, a thicker anteriorly displaced and more anteriorly inserted iris and anteriorly positioned ciliary body and its processes, and the degree of pupillary block.[7,12,16,20]

Pseudoexfoliation syndrome can be defined as a systemic pathology that is generated by the deposition of extracellular fibrillar material in different tissues, and which, depending on the affected person, can cause different subsequent entities.[21-23]

In the case of ophthalmology, pseudoexfoliation syndrome is an age-related ocular disorder characterized by extracellular fibrillar deposition on various ocular tissues. Deposits are commonly seen in the anterior segment, particularly on the lens surface and pillar rim. Histologically, the components of the exfoliative material have been found to be various basement membranes (eg, laminin, nidogen, and fibronectin), elastic fiber system (eg, fibrillin-1, elastin, and growth factor-binding proteins latent transformant) and enzymatically active components (eg, metalloproteinases, extracellular aggregates, and lysyl oxidase-like cross-linking enzyme.[21-26]

It should be noted that pseudoexfoliation syndrome and exfoliative syndrome are two different names to refer to the same clinical entity. Pseudoexfoliative glaucoma and exfoliative glaucoma are also synonymous.[21-26]

The relationship between the development of glaucoma and the presence of the pseudoexfoliative syndrome had not been previously clarified, until the development of new diagnostic techniques, the roles of said syndrome in the pathophysiology were established, as well as the roles that the cellular components in the flow of aqueous humor and how all these events can lead to irreversible damage of this pathology.[25,26]

THE RELATIONSHIP BETWEEN PSEUDOEXFOLIATION SYNDROME AND OPEN-ANGLE GLAUCOMA

Open-angle glaucoma: In patients with open-angle glaucoma, it is commonly recognized as the existence of greater resistance to the outflow of aqueous humor through the trabecular meshwork, although, as mentioned above, it is also accepted as glaucoma. open angle even when only optic nerve or nerve fiber defects are found. The problem, in the case of outflow resistance, is generated at the level of the trabeculum, whose porosity

is decreased, or beyond, in Schlemm's canal or the aqueous veins, with fluid retention and consequent increase in intraocular pressure, which on average increases between 30 to 45 mmHg.[27,29]

The lamina is the weakest point of the eye wall under constant pressure. Intraocular pressure-induced stress and strain can lead to compression, deformation, and remodeling of the cribriform plate followed by mechanical axonal damage and disruption of axonal transport, which interrupts retrograde delivery of essential trophic factors to retinal ganglion cells from its target of the brainstem (relay neurons of the lateral geniculate nucleus).[28,30]

Pseudoexfoliation syndrome is the most common determinable cause of open-angle glaucoma. The choroid is a vascular tissue that nourishes the optic nerve head and the outer layer of the retina. In addition to eye nutrition, it has important functions including volume and temperature regulation. Among glaucoma patients with similar glaucomatous damage, those with PEX material had thinner choroids compared with those without evidence of PEX material. In addition, various findings indicate that subfoveal choroidal thickness is reduced in glaucoma cases with the presence of such material, however, there was no correlation between choroidal thickness and glaucoma damage. The fact that choroidal thickness does not change in primary open-angle glaucoma, but decreases in pseudoexfoliative glaucoma, may be attributed to hemodynamic changes resulting from the effect of exfoliative material on vascular structures.[23,31-34]

THE RELATIONSHIP BETWEEN PSEUDOEXFOLIATION SYNDROME AND ANGLE-CLOSURE GLAUCOMA

Angle-closure glaucoma: The distinguishing feature of primary angle-closure glaucoma with respect to primary open-angle glaucoma is that the site of outflow of aqueous humor in the eye is obstructed by the apposition of the iris, a fact that results in a angular sharpening, i.e. an anatomically closed one (by definition at least 270° of the angle is occluded). The structures described at the level of the chamber angle may be normal, but the root of the iris is attached to the posterior face of the cornea, causing a narrowing to a greater or lesser extent. This folding of the root of the iris to the posterior corneal face can be explained by different disorders, such as a laxity of the irradiated tissue, vascular disorders, etc. The intraocular pressure increases in this case on average between 45 to 60 mmHg, this being the result of a mechanical occlusion.[28,35,36]

The angle can often be narrow or occluded in cases of pseudoexfoliation syndrome. The prevalence of occludeable angles varies by study, but in some studies the occurrence of angle closure was found to be 2.2%.[37-41]

The development of closed angle closure in one patient was attributed to an increase in irido-lenticular adhesions secondary to the presence of material typical of the same syndrome. Evidence of pupillary block was found, therefore gonioscopy has been routinely recommended in individuals with this syndrome to monitor the angle and consider timely treatment.[38-41]

Once the pathophysiological mechanisms of both types of glaucoma are understood, it is possible to establish a relationship between these entities and the pseudoexfoliative syndrome, since a vicious circle is generated due to vascular and mechanical factors that generate cell damage and the accumulation of toxic metabolites due to the inflammation in an originally privileged site, immunologically speaking, thus, apoptotic pathways due to cell damage and necrosis are added. Following this line of ideas, some points of the pathophysiology of the pseudoexfoliative syndrome could be considered true.[42]

With the above, the existence of vascular and mechanical factors that lead to neuronal death, caused, at least in part, by a process of apoptosis, is defended. However, it seems that other additional necrosis processes can also coexist, such as accumulation of extracellular material, this is known as pseudoexfoliative syndrome.[28]

Pseudoexfoliation syndrome is defined as a systemic disorder resulting from the progressive accumulation of extracellular material on various tissues. This usually determines an increase in intraocular pressure, changes in the anatomical aspects of the optic nerve and alterations in the visual field that lead to the diagnosis of pseudoexfoliative glaucoma. In the absence of abnormalities, the creation of energy that occurs in the mitochondria causes electrons to migrate in pairs from one energy level to another.[28]

Pseudoexfoliation syndrome is an age-related systemic microfibrilopathy caused by the progressive accumulation and gradual deposition of gray and white extracellular material on various tissues.[42]

The presence of pseudoexfoliation syndrome associated with elevated levels of intraocular pressure, related alterations in the computerized perimeter examination, and/or changes in the anatomical aspects of the optic nerve determines the diagnosis of pseudoexfoliative glaucoma. In fact, pseudoexfoliative syndrome is considered one of the most common causes of glaucoma.[42]

In the case of alteration of the vascular situation, with the appearance of repercussion phenomena, the electrons only migrate one by one, not in pairs. This results in the creation of free oxygen radicals that remain free in the mitochondria. This explains the high concentrations of glutamate found in glaucomatous eyes, since free radicals prevent their reabsorption in the synaptic space, which is

normally produced by the presynaptic cell, where it is stored. Under normal physiological conditions, the bipolar cell releases glutamate as a neurotransmitter destined to stimulate the ganglion cell, where it is converted to glutamine.[28,35]

As free oxygen radicals are produced, glutamate titers in the synaptic cleft increase and the ganglion cell is stimulated too long and too intensely. This causes intracellular calcium concentrations to be very high. A massive entry of sodium into the cell leads to the sodium-calcium pump being reversed, so that this substance cannot leave the cell and the production of nitric oxide is extreme.[28]

Nitric oxide is a gaseous free radical, with an important vasodilator and neuroprotective function under normal conditions. However, in case of reperfusion its values are extremely high. It is converted to a superoxide which leads to the formation of peroxynitrite, which is very detrimental to the ganglion cell and glia, leading to neuronal degeneration.[32]

This theory would explain diffuse damage to the ganglion cells, but in reality the lesion is characterized by sectoral lesions of the fibers at their entry into the optic nerve. Therefore, the neuronal suffering described must be accompanied by a more selective axonal damage that occurs in the cribriform plate, probably due to a mechanical blockade of axonal transport caused by intraocular pressure that would alter the microtubules, or due to a reduction in the vascular supply. with a decrease in the energy input necessary for the maintenance of transport systems.[28]

There has been much speculation that the thicker fibers of the optic nerve (magnocellular system) are affected earlier than the thinner ones (parvocellular system). However, this fact may simply be due to the fact that the papillary areas that are initially affected correspond to peripheral regions, where fibers with a larger diameter abound, while the papillomacular bundle, made up of central parvocellular fibers responsible for visual acuity, is affects late. Recent studies have not been able to demonstrate a selective affectation of these systems or of the cell conium "in charge of blue vision" in experimental glaucomas in monkeys 6, so that it may simply be an erroneous conclusion conditioned by the topography of the defects.[28]

There is evidence that immune mechanisms play some role in glaucoma-induced damage. Antibodies to heat proteins and autoantibodies are present in higher concentrations in glaucoma patients compared to those without. Heat proteins have been shown to have a protective effect against cellular stress and are present in high concentrations. concentrations in early glaucoma. Antibody inhibition by injection of anti-T cell antibodies or by COP 1 vaccination slows or stops ganglion cell apoptosis in experimental glaucoma. COP-1 is a synthetic copolymer made up of the amino acids Ala, Lys, Glu and Tyr, which is used as an immunosuppressive drug, it can induce a response mediated by passive or active T cells which is neuroprotective.[35] It can also cause what is known as pseudoexfoliation syndrome, which is a common age-related pathology characterized by the progressive production and accumulation of extracellular fibrillar material in different tissues, and is frequently associated with chronic severe open-angle glaucoma and waterfall. Pseudoexfoliation syndrome affects 30% of people over 60 years of age with a worldwide distribution and is diagnosed by biomicroscopy when abnormal fibrillar deposits are seen in ocular structures of the anterior segment. Pseudoexfoliation syndrome has been recognized for at least 90 years as a cause of glaucoma, associated with characteristic changes of the anterior surface of the lens capsule. Characteristic alterations of ocular tissues predispose to many intraocular complications including phacodonesis, lens subluxation, angle-closure glaucoma, pigment dispersion, poor mydriasis, blood-aqueous barrier dysfunction, posterior synechiae, and corneal decompensation.[42,43]

These alterations also explain the wide range of complications that occur in association with intraocular surgery in patients with pseudoexfoliation syndrome, including zonular dehiscence, vitreous loss with posterior capsule rupture, iris hemorrhage, corneal endothelial decompensation, postoperative inflammation, peaks of ocular hypertension, secondary cataract and dislocation of intraocular implants.[43,44]

In summary, it could be roughly described, the pathophysiology of the pseudoexfoliation syndrome is associated with excessive production of micro elastic fibrillin components, enzymatic processes, overexpression of TGF-B1, a proteolytic imbalance between MMPs and TIMPs, inflammatory process, increased oxidative and cellular stress as well as an insufficient cellular response to stress, which is reflected in poor regulation of antioxidative enzymes. The exact chemical composition of the pseudoexfoliation material is still unknown. However, the pathological process is characterized by the chronic accumulation of an abnormal fibrillar matrix product, which is also the result of excessive production or insufficient elimination, making it pathognomonic.[43-50]

CONCLUSION

Glaucoma is a pathology that is constantly increasing and of important clinical relevance due to the irreversible blindness that it can cause. The early identification as well as the understanding of the pathophysiology of this entity should be the work of health personnel. The pathophysiological process that takes place is a series of events that end up triggering a dysfunction of the epithelium and structures, causing intraocular pressure to increase and causing corneal damage. Corneal damage associated with pseudoexfoliation is probably of

multifactorial aetiology. There are several theories as to why this endotheliopathy develops, including penetration of pseudoexfoliation material into Descemet's membrane breaking hexagonal connections and endothelial layer signaling and promoting apoptosis, hypoxia to the anterior chamber with increased antioxidant stress and reduced of ascorbic acid. Glaucoma progression and its sequelae may be more related to higher intraocular pressures than to other mechanisms. Various studies relate oxidative stress to glaucomatous progression. As the composition of the material causing pseudoexfoliation is further studied, its influence on the eye can be better understood. It would be interesting to evaluate its role in glaucomatous optic neuropathy in patients with pseudoexfoliation syndrome.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Johnson M, McLaren JW, Overby DR. Unconventional aqueous humor outflow: A review. Exp Eye Res. 2017;158:94-111.
2. Costagliola C, dell'Omo R, Agnifili L, Bartollino S, Fea AM, Uva MG, et al. How many aqueous humor outflow pathways are there? Surv Ophthalmol. 2020;65(2):144-70.
3. Wang Q, Thau A, Levin AV, Lee D. Ocular hypotony: A comprehensive review. Surv Ophthalmol. 2019;64(5):619-38.
4. Sánchez MGJ, Del Pozo EC, Medina RJA, Naude J, Solorzano BA. Numerical simulation of the aqueous humor flow in the eye drainage system; a healthy and pathological condition comparison. Med Eng Phys. 2020;83:82-92.
5. Carreon TA, Edwards G, Wang H, Bhattacharya SK. Segmental outflow of aqueous humor in mouse and human. Exp Eye Res. 2017;158:59-66.
6. Carreon T, van der Merwe E, Fellman RL, Johnstone M, Bhattacharya SK. Aqueous outflow - A continuum from trabecular meshwork to episcleral veins. Prog Retin Eye Res. 2017;57:108-33.
7. Dvoriashyna M, Repetto R, Romano MR, Tweedy JH. Aqueous humour flow in the posterior chamber of the eye and its modifications due to pupillary block and iridotomy. Math Med Biol. 2018;35(4):447-67.
8. Acott TS, Vranka JA, Keller KE, Raghunathan V, Kelley MJ. Normal and glaucomatous outflow regulation. Prog Retin Eye Res. 2021;82(100897):100897.
9. Lusthaus J, Goldberg I. Current management of glaucoma. Med J Aust. 2019;210(4):180-7.
10. Geyer O, Levo Y. Glaucoma is an autoimmune disease. Autoimmun Rev. 2020;19(6):102535.
11. Jonas JB, Aung T, Bourne RR, Bron AM, Ritch R, Panda-Jonas S. Glaucoma. Lancet. 2017;390(10108):2183-93.
12. Zukerman R, Harris A, Vercellin AV, Siesky B, Pasquale LR, Ciulla TA. Molecular genetics of glaucoma: Subtype and ethnicity considerations. Genes (Basel). 2020;12(1):55.
13. Aggarwala KRG. Ocular accommodation, intraocular pressure, development of myopia and glaucoma: Role of ciliary muscle, choroid and metabolism. Med Hypothesis Discov Innov Ophthalmol. 2020;9(1):66-70.
14. News.un.org. Available at: https://news.un.org/es/story/2009/03/1158791. Accessed on 8 November 2021.
15. Who.int. Available at: https://www.who.int/es/news-room/fact-sheets/detail/blindness-and-visual-impairmentdel. Accessed on 8 November 2021.
16. Guo T, Guo L, Fan Y, Fang L, Wei J, Tan Y, et al. Aqueous humor levels of TGFβ2 and SFRP1 in different types of glaucoma. BMC Ophthalmol. 2019;19(1):170.
17. Sun X, Dai Y, Chen Y, Yu D-Y, Cringle SJ, Chen J, et al. Primary angle closure glaucoma: What we know and what we don't know. Prog Retin Eye Res. 2017;57:26-45.
18. Org.co. Available at: http://www.scielo.org.co/scielo.php?script=sci_arttext&pid=S0120-00112017000500059&lang=pt. Accessed on 8 November 2021.
19. Liu S-A, Zhao Z-N, Sun N-N, Han Y, Chen J, Fan Z-G. Transitions of the understanding and definition of primary glaucoma. Chin Med J (Engl). 2018;131(23):2852-9.
20. Tanner L, Gazzard G, Nolan WP, Foster PJ. Has the EAGLE landed for the use of clear lens extraction in angle-closure glaucoma? And how should primary angle-closure suspects be treated? EYE. 2020;34(1):40-50.
21. Palko JR, Qi O, Sheybani A. Corneal alterations associated with pseudoexfoliation syndrome and glaucoma: A literature review. J Ophthalmic Vis Res. 2017;12(3):312-24.
22. McMonnies CW. Glaucoma history and risk factors. J Optom. 2017;10(2):71-8.
23. Turgut Coban D, Cakir T, Erol MK, Dogan G, Dogan B, Bilgilisoy Filiz M, et al. Electroneuromyographic findings in pseudoexfoliation syndrome. Int Ophthalmol. 2018;38(2):705-12.
24. Sakurada Y, Mabuchi F. Genetic risk factors for glaucoma and exfoliation syndrome identified by genome-wide association studies. Curr Neuropharmacol. 2018;16(7):933-41.
25. Aviv U, Ben Ner D, Sharif N, Gur Z, Achiron A. Pseudoexfoliation: An ocular finding with possible systemic implications. Isr Med Assoc J. 2017;19(1):49-54.
26. Shumway C, Curtin K, Taylor S, Sundar KM, Wirostko BM, Ritch R. Association between

obstructive sleep apnea and exfoliation syndrome: The Utah project on exfoliation syndrome. Ophthalmol Glaucoma. 2021;4(3):260-7.
27. Evangelho K, Mogilevskaya M, Losada-Barragan M, Vargas-Sanchez JK. Pathophysiology of primary open-angle glaucoma from a neuroinflammatory and neurotoxicity perspective: a review of the literature. Int Ophthalmol. 2019;39(1):259-71.
28. Flammer J, Orgül S, Costa VP, Orzalesi N, Krieglstein GK, Serra LM, et al. The impact of ocular blood flow in glaucoma. Prog Retin Eye Res. 2002;21(4):359-93.
29. Murphy ML, Pokrovskaya O, Galligan M, O'Brien C. Corneal hysteresis in patients with glaucoma-like optic discs, ocular hypertension and glaucoma. BMC Ophthalmol. 2017;17(1):1.
30. Flammer J, Haefliger IO, Orgül S, Resink T. Vascular dysregulation: a principal risk factor for glaucomatous damage? J Glaucoma. 1999;8(3):212-9.
31. Çınar E, Yüce B, Aslan F. Retinal and choroidal vascular changes in eyes with Pseudoexfoliation syndrome: A comparative study using optical coherence tomography angiography. Balkan Med J. 2019;37(1):9-14.
32. Aydın Yaz Y, Yıldırım N, Yaz Y, Tekin N, İnal M, Şahin FM. Role of oxidative stress in pseudoexfoliation syndrome and pseudoexfoliation glaucoma. Turk J Ophthalmol. 2019;49(2):61-7.
33. Terracciano L, Cennamo M, Favuzza E, Julia L, Caporossi O, Mencucci R. An in vivo confocal microscopy study of corneal changes in pseudoexfoliation syndrome. Eur J Ophthalmol. 2019;29(5):555-60.
34. Kan E, Yılmaz A, Demirağ MD, Çalık M. Is pseudoexfoliation syndrome a risk factor for cerebro vascular disease? Semin Ophthalmol. 2017;32(2):153-6.
35. Montero MÁP, Amézquita MGX. Glaucoma agudo por cierre angular: manejo de urgencias por el optómetra. Cienc tecnol para salud vis ocul. 2014;12(1):107.
36. Quigley HA, Sanchez RM, Dunkelberger GR, L'Hernault NL, Baginski TA. Chronic glaucoma selectively damages large optic nerve fibers. Invest Ophthalmol Vis Sci. 1987;28(6):913-20.
37. Desai MA, Lee RK. The medical and surgical management of pseudoexfoliation glaucoma. Int Ophthalmol Clin. 2008;48(4):95-113.
38. Tarkkanen A. Pseudoexfoliation of the lens capsule. A clinical study of 418 patients with special reference to glaucoma, cataract, and changes of the vitreous. Acta Ophthalmol Suppl. 1962;71:1-98.
39. Wishart PK, Spaeth GL, Poryzees EM. Anterior chamber angle in the exfoliation syndrome. Br J Ophthalmol. 1985;69(2):103-7.
40. Franks WA, Miller MH, Hitchings RA, Jeffrey MN. Secondary angle closure in association with pseudoexfoliation of the lens capsule. Acta Ophthalmol (Copenh). 1990;68(3):350-2.
41. Ritch R. Exfoliation syndrome and occludable angles. Trans Am Ophthalmol Soc. 1994;92:845-944.
42. Aao.org. Available at: https://eyewiki.aao.org/Pseudoexfoliative_Glaucoma. Accessed on 8 November 2021.
43. Ringvold A. A preliminary report on the amino acid composition of the pseudo-exfoliation material (PE material). Exp Eye Res. 1973;15(1):37-42.
44. Yousuf S. Ocular profile of patients with pseudoexfoliation syndrome and pseudoexfoliation glaucoma. J med sci clin res. 2018;6(11).
45. Schlötzer-Schrehardt UM, Dörfler S, Naumann GO. Corneal endothelial involvement in pseudoexfoliation syndrome. Arch Ophthalmol (Chicago, Ill 1960). 1993;111(5):666-74.
46. Naumann GO, Schlötzer-Schrehardt U. Keratopathy in pseudoexfoliation syndrome as a cause of corneal endothelial decompensation: A clinicopathologic study. Ophthalmology. 2000;107(6):1111-24.
47. Schlötzer-Schrehardt U. Genetics and genomics of pseudoexfoliation syndrome/glaucoma. Middle East Afr J Ophthalmol. 2011;18(1):30-6.
48. Izzotti A, Bagnis A, Sacca S. The role of oxidative stress in glaucoma. Mutat Res Mutat Res. 2006;612(2):105-14.
49. Tezel G. Oxidative stress in glaucomatous neurodegeneration: Mechanisms and consequences. Prog Retin Eye Res. 2006;25(5):490-513.
50. Mumcu UY, Kocer I, Ates O, Alp HH. Decreased paraoxonase1 activity and increased malondialdehyde and oxidative DNA damage levels in primary open angle glaucoma. Int J Ophthalmol. 2016;9(10):1518-20.

Cite this article as: Orozco CAO, Gutiérrez FO, Torres JMZ, Fernandez CN, Gomez AB, Aguilar SVG et al. The role of the pseudoexfoliative syndrome as a transitional entity to glaucoma. Int Surg J 2022;9:1377-82.